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TITLE: UREA AND TOTAL URINARY NITROGEN AS MEASURES OF PROTEIN CATABOLISM IN NEUROLOGIC PATIENTS

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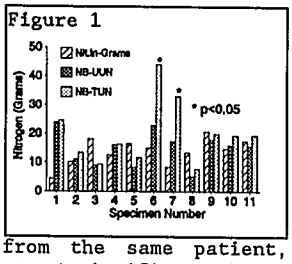
Patients with neurologic diseases undergo changes in intermediary metabolism consistent with excessive catabolism. They have rapid[1], sustained[2] rises in energy expenditure and protein wasting. Despite aggressive management, positive nitrogen balance (NB) is often difficult to maintain. The explanation is complex, but may relate to the estimation of protein requirements by NB. NB is usually calculated from 24 hour urinary urea nitrogen excretion (UUN)[3]. This study investigates the accuracy of UUN compared to simultaneous total urinary nitrogen excretion (TUN) in estimating NB in 8 patients in an intensive care unit.

Patients had a variety of disorders including CVA, head injury, and meningitis. All had Coma Scales of 6 to 8. 24 hour urine was collected according to standard ICU nutritional management and used for measurements of UUN by the urease[5] and TUN by a chemi-luminescent method[6] (Antek, Houston, TX). Nitrogen intake was calculated during urine collection. Results were compared using paired t-tests and regression analysis. Differences were considered significant at $p<0.05$.

Results for individual subjects are shown (Figure 1). UUN and TUN were similar and highly correlated in all samples but 6 and 7 ($r^2=.94$, $p<.05$). In 6 and 7, UUN significantly underestimated nitrogen loss ($p<0.05$). Specimens 4 and 6 were from the same patient, approximately two weeks apart. A significant change in UUN-TUN correlation and excretion occurred during this time.

Figure 1



Nitrogen is excreted in other forms (urate, creatinine, and ammonia). Therefore, UUN normally underestimates actual protein catabolism. Based on this data, however, it is usually reasonable to add a 4 gram correction factor to UUN to account for this difference. Clearly, this may still underestimate loss. If prealbumin, transferrin or other nutritional markers remain abnormal despite adequate feeding, it is important to measure TUN.

Despite adequate protein intake (82 ± 27 GM/day), most subjects manifested negative, or only slightly positive NB with both methods. UUN (14.9±5.9 GM/day) underestimated nitrogen losses by 0.5-47.7% compared to TUN (19.9±10.8 GM/day). A 50% underestimate would be an average of ≈131 GM of protein or ≈500 GM of skeletal muscle per day.

In summary, TUN offers a better estimate of daily nitrogen losses than UUN. Additionally, the cost of TUN measurements (≈$1.00/sample) is much cheaper, and less cumbersome than that used for estimates of UUN (≈$7.50/sample).

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TITLE: RELEASE OF CYTOKINES IN PLASMA AND LYMPH DURING ADULT RESPIRATORY DISTRESS SYNDROME COMPLICATING NECROTIZING PANCREATITIS.

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Cytokines and neutrophils are known to play a major role in the mechanisms of lung injury in adult respiratory distress syndrome[1] (ARDS). In necrotizing pancreatitis (NP), the alveolar-capillary membrane injury is usually attributed to a distinct form of lung injury resulting from a systemic release of active enzymes and vasoactive substances by the altered pancreas[2]. Drainage of thoracic duct lymph has been proposed since these toxic products gain access to the systemic circulation mainly by retroperitoneal lymphatics and the thoracic duct[3]. The aim of this study was to evaluate the release of cytokines and neutrophils enzymes in plasma and lymph of patients with ARDS complicating NP.

After informed consent and Institutional Approval, five patients with NP requiring thoracic duct drainage were studied in the first 36 hours of ARDS (D1), at day 5 (D5) and day 8 (D8). Plasma and lymph samples were assayed for tumor necrosis factor alpha (TNFα) and interleukin-6 (IL-6) (immunoradiometric assay); lactoferrin (Elisa) and myeloperoxydase activity (spectrophotometry) as a reflect of neutrophils activity, and trypsin (radioimmunoassay) as a reflect of the release of pancreatic enzymes. Data (mean±SEM) were examined using the Mann-Whitney U test and the Wilcoxon test ($p<0.05$ significant).

As soon as D1, we recorded high plasma levels of cytokines, myeloperoxydase and trypsin activity which remained unchanged for 8 days (Table 1). Plasma and lymph levels of lactoferrin remained stable within the normal range. Concentrations of mediators and toxins in lymph were not different from those measured in plasma (Table 2).

Table 1: Plasma products in necrotizing pancreatitis.

	D1	D5	D8
TNFα (N<15 pg/ml)	57±12	38±23	63±29
IL-6 (N<15 pg/ml)	1700±97	2170±170	1075±880
Myeloperoxydase (N=0 nmol/ml)	5.9±3.8	11.6±11	8.8±4.6
Lactoferrin (N<700 ng/ml)	369±97	421±29	344±58
Trypsin (N=30 ng/ml)	1534±306	1528±142	1500±624

Table 2: Lymph products in necrotizing pancreatitis.

	D1	D5	D8
TNFα (N<15 pg/ml)	62±15	42±38	63±27
IL-6 (N<15 pg/ml)	2085±36	2206±61	1624±472
Myeloperoxydase (N=0 nmol/ml)	4.9±2.9	5.5±5	8.6±7.2
Lactoferrin (N<700 ng/ml)	682±250	217±21	638±331
Trypsin (N=30 ng/ml)	1610±314	1339±200	1405±373

We conclude that a prolonged release of cytokines, neutrophils enzymes and trypsin occurs in ARDS complicating NP. The respective role of systemic and pancreatic mediators in the genesis of ARDS remains to be clarified in NP. The removal of cytokines from the thoracic lymph before systemic release might be an additional argument for the usefulness of thoracic duct drainage in the treatment of ARDS associated with NP.

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